REMARKS

Introductory Matters

Claims 1-21, 23-27, and 29-39 are pending in this application. Applicants acknowledge with appreciation that the Examiner has allowed claims 1-18.

The Office Action

35 U.S.C. § 112, first paragraph

Claims 19-21, 23-27, 29, and 32-39 stand rejected under 35 U.S.C. § 112, first paragraph as lacking enablement. The Examiner contends that the specification "while being enabling for the treatment of diabetes, or lowering blood levels of glucose" is not enabling for the other recited diseases. According to the Examiner, the treatment of some diseases is inconsistent with the treatment of other diseases. For example, the Examiner contends that "it would be impossible for a drug to treat cancers, and baldness, viral, and autoimmune diseases." Furthermore, according to the Examiner, the "specification shows inhibitory activity for Aurora-2, GSK-3, and Tau protein" but no evidence for the treatment of "osteoporosis, AML, MS, schizophrenia, Parkinson's disease, Huntington's disease, cardiomycete hypertrophy, cystic fibrosis, hepatomegaly, baldness, viral disease, autoimmune disease, [and] cancers." The Examiner concludes that practicing the claimed methods "would require undue experimentation for a skilled clinician to safely and effectively administer the claimed compounds in patients. Applicants traverse.

First, applicants respectfully note that claims 19, 20, 26, 27, 32-34, and 36 do not relate to the treatment of any recited diseases. Because these claims do not relate to the treatment of any recited disease, applicants respectfully request that the Examiner withdraw these rejections.

Additionally, applicants respectfully submit that the rejected claims are supported by the specification. As

detailed below, the biological activity of applicants' compounds (e.g., GSK-3 inhibition) has been correlated to the treatment of the claimed diseases. Some of the inconsistencies alleged by the Examiner could be due to side-effects of known drugs.

Furthermore, recent advances in the kinase art allow better understanding of the underlying mechanisms of diseases such as cancer, neurodegenerative disorders, bone disorders, and autoimmune disorders. These advances were state of the art at the time of filing and such advances are described in the background section of the specification of the instant invention. See page 2, line 12 through page 6, line 4. Specifically, the development and study of kinase-deficient animals provide a direct link between the inhibition of a kinase target and the diseases associated with that target. Soriano *et al.* found that Src-deficient mice develop osteoporosis and thus directly linked Src inhibition to the treatment of osteoporosis and other bone-loss disorders. Furthermore, Wiener *et al.* and Staley *et al.* showed that antisense Src expressed in ovarian and colon tumor cells inhibits tumor growth and thus clearly linking the inhibition of Src kinase with the treatment of ovarian and colon cancer.

Correlation for the other diseases and conditions recited in rejected claims can be found throughout the specification as originally filed. For example, it has been shown that the phosphorylation of β-catenin by GSK-3 is associated with increased neuronal cell death and, accordingly, the inhibition of GSK-3 is useful for treating neurological and neurodegenerative disorders. See page 5, lines 1-8. Furthermore, applicants respectfully point out that a well known characteristic of Alzheimer's disease relates to β-amyloid peptide and the formation of intracellular neurofibrillary tangles caused by the abnormal phosphorylation of Tau protein. See page 4, lines 20-33. As disclosed in the background section of the specification, GSK-

3 has been shown to play a key role in this abnormal phosphorylation of Tau protein in both *in vitro* and *in vivo* models. Id.

Accordingly, although the Examiner asserts that the specification is not enabling for the treatment of the diverse disorders of the instant claims, applicants respectfully submit that the models that made up the state of the art at applicants' filing date do indeed correlate inhibition of Aurora-2, GSK-3, Src, ERK-2, AKT, Tau protein, and β-catenin with the treatment of the disorders of the instant claims.

The Examiner contends that factors such as claim breadth, "amount of direction or guidance presented", and the "state of the prior art", are sufficiently lacking such that the "unpredictable nature of the art" renders the specification non-enabling for the claimed invention. Applicants would like to point out that the MPEP states that "if the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the Examiner has evidence that the model does not correlate." MPEP § 2164.02. Because the models cited in the background section of the present application do correlate the inhibition of protein kinases with the diseases recited by the instant claims, those claims are indeed enabled. Only a reasonable correlation is required - the test does not have to be highly predictive.

Enablement requires an applicant to provide sufficient guidance so that one of skill in the art may use the invention. The MPEP states that "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." See MPEP § 2164.06. Applicants do in fact provide sufficient direction and guidance in their specification as originally filed. Specifically, applicants provide the tools to make the compounds of the instant invention (see, e.g., page 210, 23 to page 311, line 6), assess the activity of those compounds

(see, e.g., page 311, line 8 to page 320, line 22, and use the compounds (see, e.g., page 16, line 25 to page 31, line 15).

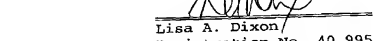
Accordingly, applicants respectfully submit that claims 19-21, 23-27, 29, and 32-39 are indeed enabled because the *in vitro* data, correlating references, and methods provided in the instant specification support the *in vivo* applications of the instant claims to treatment of diseases and other uses recited in these claims. Because the Examiner has not provided evidence that there is no correlation between the inhibition of Aurora-2, GSK-3, Src, ERK-2, AKT, Tau protein, and β-catenin and the methods recited in claims 19-21, 23-27, 29, and 32-39, applicants respectfully submit that the Examiner has not established a *prima facie* case for non-enablement. For all of the above reasons, applicants respectfully request that the Examiner withdraw these rejection.

Claims 30 and 31 stand "objected to as being dependent upon a rejected base claim." Applicants acknowledge that these claims "would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims." In view of their above arguments, applicants submit that claims 30 and 31 depend from allowable claims. Accordingly, applicants request that the Examiner withdraw these objections.

Conclusion

Accordingly, applicants request that the Examiner consider the foregoing remarks, and allow the pending claims to issue.

Respectfully submitted,



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